PCT/CH2003/000435

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P1222PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CH2003/000435	International filing date (*day/month/year*) 02 July 2003 (02.07.2003)	Priority date (*day/month/year*) 16 July 2002 (16.07.2002)
International Patent Classification (IPC) or national classification and IPC C07J 73/00		
Applicant SIEGFRIED GENERICS INTERNATIONAL AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22 January 2004 (22.01.2004)	20 October 2004 (20.10.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/CH2003/000435

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☒ the description:

pages 1-17, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☒ the claims:

pages 1-21, as originally filed

pages _____, as amended (together with any statement under Article 19

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

See the supplemental sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/CH 03/00435

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-21	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-21	NO
Industrial applicability (IA)	Claims	1-21	YES
	Claims		NO

2. Citations and explanations

The closest prior art in relation the present claimed invention is:

D1: EP-A-428 366

The following documents are also important in evaluating the inventive step of the present claimed invention:

D2: Tett. Lett. vol. 25(42), 4783-4786 (1984)
D3: US-A-5 710 342

Novelty (PCT Article 33(2))

Claim 1 relates to a process for introducing a 1,2 double bond into 4-azasteroid compounds (i.e. converting 1,2-saturated 4-azasteroids of formula (II) into corresponding 1,2-unsaturated compounds of formula (I)). This process consists of three steps:

(A) introduction of a 3-oxo protective group into an intermediate of formula III comprising an enol group (i.e. a group of the formula 2,3-en-3-O-[protective group]);

(B) introduction of the 1,2 double bond by dehydrogenating the intermediate of formula III in the presence of:

(i) a dehydrogenation catalyst, and
(ii) - an optionally substituted benzoquinone
- allyl methylcarbonate,
- allyl ethylcarbonate and/or
- allyl propylcarbonate;

(C) deprotection.

The applicant should note here that D1 (example 1) describes a process wherein:

(1) treating the 3-oxo group of the compound 17β-[t-butylaminocarbonyl]-4-azaandrost-3-on (identical with the starting product of formula (II) in claim 1) with $(COCl)_2$ in the presence of CH_2Cl_2 and pyridine protects said group, the protected intermediate derived therefrom being identical with the intermediates of formula (III) in claim 1 (in formula (III) R_3 and R_4 together represent a group of the formula -C(O)-C(O));

(2) the protected intermediate produced in step (A) is reacted with Br_2 to give the corresponding 2-bromo compound;

(3) the 2-bromo compound is deprotected to give the compound 2-bromo-17β-[t-butylaminocarbonyl]-4-azaandrost-3-on;

(4) the compound 2-bromo-17β-[t-butylaminocarbonyl]-4-

azaandrost-3-on is dehydrohalogenated to give the compound 17β-[t-butylaminocarbonyl]-4-azaandrost-1-en-3-on.

The applicant should note here that in claim 1 the 1,2 double bond is introduced using a dehydrogenation catalyst in the presence of an optionally substituted benzoquinone, allyl methylcarbonate, allyl ethylcarbonate and/or allyl propylcarbonate. In the process described in D1, Br_2 is used as a dehydrogenating agent. The process described in claim 1 and claims 2-21, which are dependent on claim 1, is therefore novel according to PCT Article 33(2).

Inventive step (PCT Article 33(3))

The problem addressed by the subject matter of the present invention consists in introducing a 1,2 double bond into 4-aza-3-on steroid compounds (see the description, page 1, line 14 to page 2, line 2).

The process claimed in claim 1 differs from that in D1 only in that, in claim 1, the 1,2 double bond is introduced using a dehydrogenation catalyst in the presence of an optionally substituted benzoquinone, allyl methylcarbonate, allyl ethylcarbonate and/or allyl propylcarbonate, whereas in D1 Br_2 is used as a dehydrogenating agent without a catalyst (see "Novelty" above).

The applicant should note here that the use of a dehydrogenation catalyst in the presence of allyl methylcarbonate to dehydrogenate carboxyl-derived protected enol intermediates is known from D2 (see D2, page 4783, figure; the dehydrogenation catalyst in D2 is

$Pd(OAc)_2$, which is identical with the preferred Pd(II) dehydrogenation catalysts indicated in dependent claim 14). Transferring this teaching from D2 to that of D1, thereby substituting the dehydrogenation catalyst used in D2 (and in claim 1) for Br_2 as used in D1 in a process carried out in the presence of allyl methylcarbonate, represents an obvious solution to the above-indicated problem, leading to a process identical with that of claim 1. Thus, the process described in claim 1 represents an obvious solution to the above-indicated problem and consequently lacks inventive step according to PCT Article 33(3).

Dependent claims 2-21 do not appear to contain any further features whereby these claims could meet the requirement for inventive step. Thus, the subject matter of these claims also lacks inventive step according to PCT Article 33(3).

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The expression "*dehydrogenation catalyst*" (claim 1) lacks a generally acknowledged meaning in this technical area and defines the catalyst by its effect, not by its chemical structure. In general, claims which attempt to characterize the invention by the result to be achieved should not be allowed (PCT Examination Guidelines, paragraph III-4.7).

However, such wording would be allowable if the invention could only be defined in this way or could not be otherwise more closely defined without the range of protection of the claims being excessively restricted **and** the result were one that could be verified by tests or procedures adequately specified in the description or known to a person skilled in the art, rather than unreasonable experiments. The applicant should note here that the structurally unlimited possibilities (claim 1 does not define any structural features of the catalyst) do not disclose a technical teaching that is sufficiently clear for said person skilled in the art to carry it out with reasonable intellectual application - the latter concept not excluding the conduct of routine experiments - because the structurally unlimited possibilities of the catalyst in claim 1 give no technical suggestion that would lead a person skilled in the art to the structural possibilities that would achieve this result. Claim 1 is thus unclear according to PCT Article 6.